American Academy of Orthopaedic Surgeons®

AAOS American Association of Orthopaedic Surgeons

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July 11, 2000

Jane E. Henney, MD
Commissioner
Food and Drug Administration (FDA)
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Dear Dr. Henney:

The American Academy of Orthopaedic Surgeons (AAOS), representing over 16,000 Board certified orthopaedic surgeons, is pleased to take this opportunity to provide additional comments on the Proposed Rule: Suitability Determination for Donors of Human Cellular and Tissue-Based Products. (Published in the Federal Register on Thursday, September 30, 1999). (Docket No. 97N-484S). This letter supplements our correspondence dated December 21, 1999, which is attached.

In our initial letter, the AAOS questioned the FDA's definition of minimally manipulated tissue, the testing of bone graft substitutes for osteoinduction, and the exemption of family-related allogeneic tissue.

To reiterate, the AAOS fellowship is supportive of the proposed rule's overall requirements. As described in the proposed rule, essentially all of the tissue banks currently involved in the processing and distribution of musculoskeletal related tissues of concern to the AAOS are already in compliance with the proposed requirements.

Upon further consideration of the proposed rule, AAOS recommends that the FDA set allowable limits for chemical additives such as glycerol, to allograft tissues. While additives do not present a problem for disease transmission, in increased concentrations, chemical additives may present a problem for potential toxicities with donor tissues. AAOS encourages the FDA to consider limits for additive substances.

AAOS shares the concern of the FDA to assure that safe and effective products enter the marketplace. We remain committed to ensuring the availability of safe tissues and tissue-based products to enhance the

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treatment of disease and injury. AAOS remains committed to protecting consumers and our patients.

Thank you for your efforts. We welcome the opportunity to work with you on this matter.

Sincerely,

William W. Tipton, Jr., MD
Executive Vice President

American Academy of Orthopaedic Surgeons®

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December 21, 1999

Jane E. Henney, MD
Commissioner
Food and Drug Administration (FDA)
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Dear Dr. Henney:

The American Academy of Orthopaedic Surgeons (AAOS), representing over 16,000 Board certified orthopaedic surgeons, is pleased to take this opportunity to comment on the Proposed Rule: Suitability Determination for Donors of Human Cellular and Tissue-Based Products. (Published in the Federal Register on Thursday, September 30, 1999). (Docket No. 97N-484S).

Inasmuch as the proposed rule enhances protections for the public regarding tissue transplantation, the AAOS fellowship is supportive of its overall requirements. As described in the proposed rule, essentially all of the tissue banks currently involved in processing and distribution of musculoskeletal related tissues of concern to the AAOS are already in compliance with the proposed requirements.

However, the AAOS would like to raise a few issues of concern with regard to FDA's regulation of human and cellular based tissue products.

First, we are unsure how the definition of "minimally manipulated tissue" may affect the FDA decisions in the regulation of particular tissue products. As it is currently written, this definition is confined to an extremely brief paragraph within the proposed rule. While the Center for Biologics, Evaluation and Research (CBER) 1997 guidance document "Proposed Approach to Regulation of Cellular and Tissue-Based Products" may provide some clarification as to what the FDA may define as "minimally manipulated tissue," the evolution of new methods, processing approaches, materials, and combinations of tissues, materials and cells, may create significant confusion or ambiguities as to what products do or do not fall within the FDA regulatory scope.

Future advancements in technologies and in the processing of human cellular and tissue-based products may put most tissue outside of the narrow definition of the proposed rule when in fact, a broader definition of "minimally

manipulated tissue," may be more appropriate. The Academy suggests that substantially more detailed guidance regarding this definition needs to be developed prior to the implementation of the rule.

Of additional concern, is that there is no requirement for osteoinductive bone graft substitutes derived from human tissues by minimally manipulative procedures to be tested for osteoinductive capacity by bioassay. The American Society for Testing and Materials (ASTM) has recently developed a draft standard for the testing of osteoinduction. Inclusion of an accepted standard may enhance public protection by providing improved quality control.

Finally, it is not clear why family-related allogeneic tissue donation is exempted from donor suitability requirements, particularly in light of potential social factors which may impair thorough disclosure of possible health-related risk factors in donor screening.

We share the concerns of the FDA in ensuring that safe and effective products enter the marketplace. We remain committed to ensuring the availability of safe tissues and tissue-based products to enhance the treatment of disease and injury and remain committed to protecting consumers and our patients.

Thank you for your efforts. We welcome the opportunity to work with you on these matters.

Sincerely,

William W. Tipton, MD

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Executive Vice President

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